

Patentanwälte

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Translation of the amended claims

- 1. Method for detecting a nucleotide sequence in a nucleic acid molecule comprising the following steps:
 - (a) hybridization of nucleic acid molecules to a set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes;
 - (b) separation of the probes that were not hybridized;
 - (c) detachment of a specifically hybridized probe in a solvent;
 - (d) analysis of the hybridized probes in a solution by means of electrospray mass spectrometry; and
 - (e) determination of the nucleic acid molecules by means of the probes hybridized to them.
- 2. Method according to claim 1, wherein the nucleic acid molecules are immobilized at the surface of a support before or after step (a).
- 3. Method according to claim 2, wherein the immobilization of the nucleic acid molecules at the surface is carried out via an NH₂, epoxy or SH function by means of coating the surface of the probe supports with a silicate or silane, via a protein-substrate, protein-protein or a protein-nucleic acid interaction or via an interaction of two hydrophobic building blocks.
- 4. Method according to claim 3, wherein the protein-substrate interaction is a biotin-streptavidin bond or an antibody-antigen bond.
- 5. Method according to claim 3, wherein the protein-nucleic acid interaction is a Gene32-nucleic acid bond.
- 6. Method according to any one of claims 1 to 5, wherein the probes are nucleic acids having a mass tag.

- 7. Method according to claim 6, wherein the mass tag is at the same time a charge tag.
- 8. Method according to claim 6, wherein the nucleic acids moreover have a charge tag.
- Method according to any one of claims 1 to 8, wherein the probes are modified nucleic acid molecules.
- 10. Method according to claim 9, wherein the modified nucleic acid molecules are PNAs, alkylated phosphorothicate nucleic acids or alkylphosphonate nucleic acids.
- 11. Method according to any one of claims 1 to 10, wherein the probes are generated by means of combinatorial solid phase synthesis.
- 12. Method according to claim 11, wherein different base building blocks are labelled in such a way that the probes synthesized therefrom can be differentiated in the mass spectrometer due to their mass.
- 13. Method according to claim 12, wherein the labelling is a methyl, ethyl, propyl, a branched or non-branched alkyl, a halogen substituted branched or non-branched alkyl, alkoxyalkyl, alkylaryl, arylalkyl, alkoxyaryl or aryloxyalkyl group or one of their deuterated or other isotopic variants.
- 14. Method according to any one of claims 10 to 13, wherein the probes have at least one modification in a defined position away from randomized nucleotides allowing for the cleavage of the probe.
- 15. Method according to claim 14, wherein modification means the introduction of a phosphorothicate group and/or an RNA base and/or a phosphotriester bond into the probe.

- 16. Method according to any one of claims 1 to 15, wherein the probes are generated as partial libraries having different mass and/or charge tags.
- 17. Method according to any one of claims 1 to 16, wherein the positions of the probes on the probe support allow for an allocation to the nucleic acid molecules hybridizing thereto.

18. Kit comprising

- (a) a set of probes as defined in any one of claims 6 to 16 and/or
- (b) a probe support which has been pretreated and thus allows for the attachment of target DNAs and/or target DNAs that have already been attached.